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EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/445,289	MUKAMOLOVA ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *100509*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *126-128,131,135-139,144 and 148-159* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *126-128,131,148-150 and 157-159* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application.
6) ☐ Other: _____.

RESPONSE TO APPLICANTS' AMENDMENT

Applicants' Amendments

1) Acknowledgment is made of Applicants' amendments filed 10/22/09 and 07/06/09 in response to the non-final Office Action mailed 01/06/09.

Status of Claims

2) Claims 126, 128, 144, 148, 149 and 159 have been amended via the amendment filed 07/06/09.

Claim 129 has been canceled via the amendment filed 07/06/09.

Claims 126-128, 131, 135-139, 144 and 148-159 are pending.

Claims 126-128, 131, 144, 148-150 and 157-159 are under examination.

Substitute Sequence Listing

3) Acknowledgment is made of Applicants' substitute sequence listing which has been entered on 10/22/09.

Prior Citation of Title 35 Sections

4) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action References.

Prior Citation of References

5) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Objection(s) Moot

6) The objection to the specification made in paragraph 9 of the Office Action mailed 01/06/09 with regard to claim 129 is moot in light of Applicants' cancellation of the claim.

Objection(s) Withdrawn

7) The objection to the specification made in paragraph 7(d) of the Office Action mailed 02/01/07 and maintained in paragraph 7 of the Office Action mailed 06/09/08 and paragraph 8 of

the Office Action mailed 01/06/09 is withdrawn in light of Applicants' amendment to the sequence listing.

8) The objection to the specification made in paragraph 9 of the Office Action mailed 01/06/09 with regard to claims 128 and 159 is withdrawn in light of Applicants' amendment to the claims.

9) The objection to claim 126 made in paragraph 23 of the Office Action mailed 01/06/09 is withdrawn in light of Applicants' amendment to the claim.

Objection(s) Maintained

10) The objection to claim 144 made in paragraph 23(b) of the Office Action mailed 01/06/09 is maintained for the reasons set forth therein. Claim 144 continues to include the limitation: 'comprising a sequence selected from …. a polypeptide'. For clarity and to be consistent with the claim language used in lines 3 and 4 of claim 126, it is suggested that Applicants delete the limitation 'comprising a sequence' from lines 3 and 4 of claim 144.

Objection(s) to Specification

11) 37 CFR 1.75(d)(1) provides, in part, that 'the terms and phrases used in the claims must find clear support or antecedent basis in the description so that the meaning of the terms in the claims may be ascertainable by reference to the description.'

The instant specification is objected to for the following reason:

Claim 128, as amended, includes the limitations: 'said bacterial cells are present in a sample' and the method 'identifies a dormant, moribund or latent *Mycobacterium tuberculosis* bacterial cells in the sample'. Claim 128 depends from the amended claim 126, which requires the steps of contacting the dormant, moribund or latent *Mycobacterium tuberculosis* bacterial cells with an isolated polypeptide as recited in part (i), (ii) or (iii) and incubating the cells in culture medium containing the polypeptide, thereby resuscitating said cells. The isolated polypeptide recited in parts i), ii) and iii) of claim 126 are polypeptide variants having at least 95% sequence identity with amino acid residues 117 to 184 of SEQ ID NO: 2; having at least 95% sequence identity with SEQ ID NO: 2; and a polypeptide comprising at least amino acid residues 117-184 of SEQ ID NO: 2. Thus, the *method of resuscitating* dormant, moribund or latent *Mycobacterium tuberculosis* cells comprising contacting the dormant, moribund or latent *Mycobacterium*

tuberculosis cells present in a sample *in vitro* and incubating the cells in culture medium containing the polypeptide is required to serve as a *method of identifying* specifically 'a dormant, moribund or latent *Mycobacterium tuberculosis* bacterial cell in the sample'. Note that the sample recited in claim 128 encompasses a sample taken from a human or animal as recited in the amended dependent claim 159.

Applicants state that support for the amendment is found in Figure 10, lines 5-15 of page 44, lines 34-36 of page 21, lines 11-15 and 26 at page 18, and pages 52 and 58 of the specification. However, these parts of the specification do not provide antecedent basis for a method of resuscitating dormant, moribund or latent *Mycobacterium tuberculosis* bacterial cells comprising contacting *in vitro* the bacterial cells in a sample of or sample from a human or with an isolated at least 95% identical polypeptide variant as recited in part (i) or (ii), or an isolated SEQ ID NO: 2 lacking 1-116 and 185-188 amino acids, or a polypeptide comprising at least 117-184 amino acids of SEQ ID NO: 2 as recited or encompassed in part (iii) of claim 126, wherein the resuscitating method comprising the contacting and the incubating steps concurrently serves as a method of specifically identifying a dormant, moribund or latent *Mycobacterium tuberculosis* bacterial cell in a generic sample, or a sample from a human or an animal. Page 52 and the title of Table 1 of the specification supports the use of 'purified' RP factor from *M. luteus* for resuscitating dormant *Mycobacterium tuberculosis* cells, which purified RP factor from *M. luteus* had weaker resuscitating activity on dormant *Mycobacterium tuberculosis* cells. Page 58 also describes the effect of RP factor from *M. luteus* on the growth of dormant or latent *Mycobacterium tuberculosis* cells.

Rejection(s) Moot

12) The rejection of claim 129 made in paragraph 23(b) of the Office Action mailed 06/09/08 and maintained in paragraph 16 of the Office Action mailed 01/06/09 under 35 U.S.C. § 112, second paragraph, as being indefinite, is moot in light of Applicants' cancellation of the claim.

13) The rejection of claim 129 made in paragraph 9 of the Office Action mailed 02/01/07 and made/maintained in paragraph 18 of the Office Action mailed 06/09/08 and maintained in paragraph 17 of the Office Action mailed 01/06/09 under 35 U.S.C § 112, first paragraph, as being non-enabled with regard to the scope, is moot in light of Applicants' cancellation of the claim.

14) The rejection of claim 129 made in paragraph 19 of the Office Action mailed 01/06/09 under 35 U.S.C. § 112, first paragraph, as containing new matter, is moot in light of Applicants' cancellation of the claim.

15) The rejection of claim 129 made in paragraph 20 of the Office Action mailed 01/06/09 under 35 U.S.C. § 112, second paragraph, as being indefinite, is moot in light of Applicants' cancellation of the claim.

Rejection(s) Withdrawn

16) The rejection of claim 128 made in paragraph 23(a) of the Office Action mailed 06/09/08 and maintained in paragraph 15 of the Office Action mailed 01/06/09 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

17) The rejection of claims 126-128, 131, 144, 148-150 and 157-159 made in paragraph 9 of the Office Action mailed 02/01/07 and made/maintained in paragraph 18 of the Office Action mailed 06/09/08 and maintained in paragraph 17 of the Office Action mailed 01/06/09 under 35 U.S.C § 112, first paragraph, as being non-enabled with regard to the scope, is withdrawn in light of Applicants' amendment to the claims and/or the base claim. A new rejection under 35 U.S.C § 112, first paragraph is set forth below to address the claims as amended.

18) The rejection of claims 126, 127, 131, 144, 148 and 149 made in paragraph 14 of the Office Action mailed 02/01/07 and made/maintained in paragraph 20 of the Office Action mailed 06/09/08 and maintained in paragraph 18 of the Office Action mailed 01/06/09 under 35 U.S.C. § 102(b) as being anticipated by of Mukamolova *et al*. (*Antonie van Leeuwenhoek* 67: 289-295, 1995) (Mukamolova *et al*., 1995) as evidenced by Mukamolova *et al*. (*PNAS* 95: 8916-8921, July 1998 – Applicants' IDS) (Mukamolova *et al*., 1998), is withdrawn in light of Applicants' amendment to the claims and/or the base claim.

19) The rejection of claims 128 and 159 made in paragraph 19 of the Office Action mailed 01/06/09 under 35 U.S.C. § 112, first paragraph, as containing new matter, is withdrawn. A new rejection is set forth below to address the claim as amended.

20) The rejection of claims 157 and 158 made in paragraph 20(a) of the Office Action mailed 01/06/09 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn upon further consideration.

21) The rejection of claims 157 and 158 made in paragraph 22 of the Office Action mailed 01/06/09 under 35 U.S.C. § 103(a) as being unpatentable over Mukamolova *et al*. (*Antonie van Leeuwenhoek* 67: 289-295, 1995, of record) (Mukamolova *et al*., 1995) as applied to claims 126 and 144 above, and further in view of Harlow *et al*. (*In*: *Antibodies*: *A Laboratory Manual*. Cold Spring Harbor Laboratory, Chapter 5, 60-71, 1988), is withdrawn in light of Applicants' amendment to the claims and/or the base claim.

22) The rejection of claim 128 made in paragraph 20(c) of the Office Action mailed 01/06/09 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn. A new rejection is set forth below to address the claim as amended.

23) The rejection of claim 159 made in paragraph 20(d) of the Office Action mailed 01/06/09 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the base claim.

Rejection(s) Maintained

24) The rejection of claim 158 made in paragraph 20(b) of the Office Action mailed 01/06/09 under 35 U.S.C. § 112, second paragraph, as being indefinite, is maintained for the reasons set forth therein and herein below. Applicants have not specifically addressed this rejection. Claim 158 which includes the limitation: 'wherein the polypeptide is purified essentially to homogeneity', depends from claim 144, wherein dormant, moribund or latent bacterial cells are contacted with 'a cell strain expressing a nucleic acid encoding a polypeptide'. It remains unclear how a polypeptide that is already purified essentially to homogeneity can be encoded by the cell strain expressing a nucleic acid.

Rejection(s) Necessitated by Applicants' Amendment

Rejection(s) under 35 U.S.C § 112, First Paragraph

25) The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to

which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Rejection(s) under 35 U.S.C § 112, First Paragraph (New Matter)

26) Claims 126-128, 131, 144, 148-150 and 157-159 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 128, as amended, includes the limitations: 'said bacterial cells are present in a sample' and the method 'identifies a dormant, moribund or latent *Mycobacterium tuberculosis* bacterial cells in the sample'. Claim 128 depends from the amended claim 126, which requires the steps of contacting the dormant, moribund or latent *Mycobacterium tuberculosis* bacterial cells with an isolated polypeptide as recited in part (i), (ii) or (iii) and incubating the cells in culture medium containing the polypeptide, thereby resuscitating said cells. The isolated polypeptide recited in parts i), ii) and iii) of claim 126 are polypeptide variants having at least 95% sequence identity with amino acid residues 117 to 184 of SEQ ID NO: 2; polypeptide variants having at least 95% sequence identity with SEQ ID NO: 2; and a polypeptide comprising at least amino acid residues 117-184 of SEQ ID NO: 2. Thus, the *method of resuscitating* dormant, moribund or latent *Mycobacterium tuberculosis* cells comprising contacting the dormant, moribund or latent *Mycobacterium tuberculosis* cells present in a sample *in vitro* and incubating the cells in culture medium containing the polypeptide is required to serve as a *method of identifying* specifically 'a dormant, moribund or latent *Mycobacterium tuberculosis* bacterial cell in the sample' in the amended claim 128. Note that the sample recited in claim 128 encompasses a sample taken from a human or animal as recited in the amended dependent claim 159. The resuscitating method of claim 144 requires contacting *Mycobacterium tuberculosis* bacterial cells *in vitro* with a cell strain expressing a nucleic acid encoding a polypeptide having at least 95% sequence identity with amino acid residues 117 to 184 of SEQ ID NO: 2; having at least 95% sequence identity with SEQ ID NO: 2; and a polypeptide comprising at least amino acid residues 117-184 of SEQ ID NO: 2.

Applicants state that support for the amendment is found in Figure 10, lines 5-15 of page 44, lines 34-36 of page 21, lines 11-15 and 26 at page 18, and pages 52 and 58 of the

specification. However, these parts of the specification do not provide descriptive support for a method of resuscitating dormant, moribund or latent *Mycobacterium tuberculosis* bacterial cells comprising *in vitro* contacting of the bacterial cells in a generic sample or a sample from a human or animal with an isolated at least 95% identical polypeptide variant as recited in part (i) or (ii), or an isolated SEQ ID NO: 2 lacking 1-116 and 185-188 amino acids, or a polypeptide comprising at least 117-184 amino acids of SEQ ID NO: 2 as recited or encompassed in part (iii) of claim 126, wherein the resuscitating method comprising the contacting and the incubating steps concurrently serves as a method of specifically identifying a dormant, moribund or latent *Mycobacterium tuberculosis* bacterial cell in said sample. Page 52 and the title of Table 1 of the specification supports the use of 'purified' RP factor from *M. luteus* for resuscitating dormant *Mycobacterium tuberculosis* cells, which purified RP factor from *M. luteus* had weaker resuscitating activity on dormant *Mycobacterium tuberculosis* cells. Page 58 also describes the effect of RP factor from *M. luteus* on the growth of dormant or latent *Mycobacterium tuberculosis* cells. No isolated polypeptide having at least 95% sequence identity with amino acid residues 117-184 amino acids of SEQ ID NO: 2, or at least 95% sequence identity with SEQ ID NO: 2. or amino acids 117 to 184 of SEQ ID NO: 2, and a cell expressing a nucleic acid encoding such a polypeptide, which *concurrently* have the ability to resuscitate dormant, moribund or latent *Mycobacterium tuberculosis* cells in a generic sample or a sample from a human or animal, upon contacting the cell with said polypeptide or said cell and incubating the cells, is supported in the as-filed specification. Therefore, the identified limitation(s) in the claim(s) and the currently claimed scope of the claims constitute new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P 608.04 to 608.04(c).

Applicants are invited to point to the descriptive support in specific pages and lines of the disclosure, as originally filed, for the limitation identified above, or alternatively, remove the new matter from the claim(s). Applicants should specifically point out the support for any amendments made to the disclosure. See MPEP 714.02 and 2163.06.

Rejection(s) under 35 U.S.C § 112, First Paragraph (Written Description)

27) Claims 126-128, 131, 144, 148-150 and 157-159 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The *Written Description Guidelines* state:

> There is an inverse correlation between the level of predictability in the art and the amount of disclosure necessary to satisfy the written description requirement. For example, if there is a well-established correlation between the structure and function in the art, one skilled in the art will be able to reasonably predict the complete structure of the claimed invention from its function.

The written description requirement can be met by describing the claimed subject matter to a person skilled in the art using sufficiently detailed, relevant identifying characteristics such as functional characteristics, and correlating those functional characteristics with a disclosed structure. See *Enzo Biochem v. Gen-Probe,* 323 F.3d 956, 964, 967, 968 (Fed. Cir. 2002). Sufficient description to show possession of a genus may be achieved by means of recitation of a representative number of polypeptide species falling within the scope of the genus, or recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406. Possession may *not* be shown by merely describing how to obtain possession of members of the claimed genus or how to identify their common structural features. See *University of Rochester*, 358 F.3d at 927, 69 USPQ2d at 1895.

Claim 126, as amended, is drawn to a method of resuscitating dormant, moribund or latent *Mycobacterium tuberculosis* bacterial cells comprising contacting *in vitro* the bacterial cells with an isolated polypeptide as recited in part (i), (ii) or (iii) and incubating the cells in culture medium containing the polypeptide, thereby resuscitating said cells. The isolated polypeptide recited in parts i), ii) and iii) of claim 126 and in claims 148-150 is a polypeptide variant having at least 95% sequence identity with amino acid residues 117 to 184 of SEQ ID NO: 2; a polypeptide variant having at least 95% sequence identity with SEQ ID NO: 2; and a polypeptide comprising at least amino acid residues 117-184 of SEQ ID NO: 2 respectively. While the dependent claim 127 requires the polypeptide variants to be recombinant, the dependent claim 131 requires the

polypeptide to be present in unit dosage form and the dependent claim 157 requires the polypeptide to be purified essentially to homogeneity. Claim 128, as amended, includes the limitations: 'said bacterial cells are present in a sample' and the method 'identifies a dormant, moribund or latent *Mycobacterium tuberculosis* bacterial cells in the sample'. The *method of resuscitating* dormant, moribund or latent *Mycobacterium tuberculosis* cells of claim 128 comprising contacting the dormant, moribund or latent *Mycobacterium tuberculosis* cells present in a sample *in vitro* and incubating the cells in culture medium containing the polypeptide is required to serve as a *method of identifying* specifically 'a dormant, moribund or latent *Mycobacterium tuberculosis* bacterial cell in the sample'. Note that the sample recited in claim 128 encompasses a sample taken from a human or animal as recited in the amended dependent claim 159. The resuscitating method of claim 144 requires contacting *Mycobacterium tuberculosis* bacterial cells *in vitro* with a cell strain expressing a nucleic acid encoding a polypeptide having at least 95% sequence identity with amino acid residues 117 to 184 of SEQ ID NO: 2; having at least 95% sequence identity with SEQ ID NO: 2; and a polypeptide comprising at least amino acid residues 117-184 of SEQ ID NO: 2. The polypeptide encoded by the nucleic acid comprised within the cell strain is purified essentially to homogeneity according to claim 158. Except for the method of claims 157 and 158, the polypeptide used in the method of rest of the claims under examination is not required to be purified.

A review of the instant specification indicates that Applicants were not in possession of an *in vitro* method of resuscitating dormant, moribund, or latent *Mycobacterium tuberculosis* cells comprising contacting said bacterial cells with an isolated or purified polypeptide having at least 95% identity to SEQ ID NO: 2, or at least 95% identity with residues 117 to 184 of SEQ ID NO: 2, or having amino acid residues 117 to 184 of SEQ ID NO: 2, or with a cell strain that comprises a nucleic acid that encodes such a polypeptide, and for a method wherein the recited polypeptide results in identification of dormant, moribund, or latent *Mycobacterium tuberculosis* cells in a sample, or a sample that is from a human or animal, as claimed broadly. A polypeptide that is at least 95% identical to amino acid residues 117-184 of SEQ ID NO: 2, or at least 95% identical to SEQ ID NO: 2 is a polypeptide that is at least 5% non-identical to amino acid residues 117-184 of SEQ ID NO: 2, or at least 5% non-identical to SEQ ID NO: 2. The recited polypeptide variants represent a vast genus of polypeptide sequence variants wherein the variant are required to have

the above-identified required function. The variations within the encompassed polypeptide genus are huge. Any amino acids in any sequence along the length of SEQ ID NO: 2 or along the length of 117-184 of SEQ ID NO: 2 may be substituted as long as there is at least 95% identity to SEQ ID NO: 2. However, other than a purified SEQ ID NO: 2 which has been shown to have the capacity to resuscitate dormant, moribund or latent *M. tuberculosis* cells *in vitro* in a culture medium upon contacting and incubating with the cells, no other polypeptide variants having at least 95% identical to amino acid residues 117-184 of SEQ ID NO: 2, or at least 95% identical to SEQ ID NO: 2 and also having the functional capacity to resuscitate dormant, moribund or latent *M. tuberculosis* cells *in vitro* in a culture medium or a sample have been adequately described and their structure correlated with the requisite function. The description of a single species having the required function within the recited broad genus may not be sufficient to support the patentability of the genus under 35 U.S.C § 112, first paragraph. See *University of California v. Eli Lilly & Co*., 119 F.3d 15559, 1567, 43 USPQ2d 1398, 1405 (Fed. Cir. 1997). The instant specification does not disclose which 5% of amino acid residues should be changed within the single disclosed polypeptide species of SEQ ID NO: 2 or within amino acids 117-184 of SEQ ID NO: 2 in order to maintain the required biological function, i.e., the functional capacity to resuscitate dormant, moribund or latent *M. tuberculosis* cells *in vitro* in a culture medium or a sample, upon performing the recited steps. There is lack of adequate description of the structure of a representative number of at least 95% identical polypeptide variant species having the requisite function. It should be noted that written description requires more than a mere statement that something is a part of the invention.

With respect to the written description requirement, while 'examples explicitly covering the full scope of the claim language' typically will not be required, a sufficient number of representative species must be included 'to demonstrate that the patentee possesses the full scope of the [claimed] invention'. *Lizardtech, Inc. v. Earth Resource Mapping, Inc.*, 424 F.3d 1336, 1345, 76 USPQ2d 1724, 1732 (Fed. Cir. 2005). In the instant case, Applicants' specification does not contain adequate written description sufficient to show they had possession of the full scope of their claimed invention at the time the application was filed. The instant specification mentions of polypeptide variant having at least 95% identity to the amino acid sequence of SEQ ID NO: 2. However, the specification does not disclose a correlation between the function, i.e.,

capacity to resuscitate dormant, moribund or latent *M. tuberculosis* cells *in vitro* in a culture medium or a sample upon performing the recited steps, and the precise structure(s) responsible for that function such that the skilled artisan would have known what modifications, substitutions, or variations could be made of the large number of modifications or variations currently encompassed within the scope of the instant claims, without losing that function. This description is important because a change of even a single amino acid residue can alter the folding or conformation of a polypeptide such that the functional region no longer retains the function(s). Applicants only speculated that the cell wall lytic activity is 'likely' to be important for resuscitating dormant, moribund or latent bacterial cells. See paragraph bridging pages 13 and 14 of Applicants' amendment filed 08/01/07 and paragraph bridging pages 17 and 18 filed 10/16/08. The specific regions or amino acid residues within the amino acids spanning 117 to 184 of SEQ ID NO: 2 that are associated with the alleged capacity to resuscitate dormant, moribund or latent *M. tuberculosis* bacterial cells *in vitro* in any sample or a sample from a human or animal, are not identified, without which one of skill in the art would not be able to avoid alterations or substitutions in those regions, or among amino acid residues within positions 117 to 184 of SEQ ID NO: 2, while producing species of the genus of the recited polypeptide variants. A domain that includes four conserved tryptophan residues and two conserved cysteine residues which 'may' form a disulfide bridge (page 51, line 28 to page 52, line 2 of the specification) is not associated with the recited function of resuscitating and/or identifying dormant, moribund or latent *M. tuberculosis* bacterial cells. Even if one produced a series of polypeptide variants falling within the scope of the instant claims and used them to contact dormant, moribund or latent *M. tuberculosis* cells *in vitro*, there is no predictability that these polypeptide variants would retain the capacity to resuscitate said dormant, moribund, or latent bacterial *M. tuberculosis* bacterial cells, absent a concrete structure-function correlation. This is critically important because the state of the art at the time of the invention was limited to certain unsubstantiated or unproven speculations with regard to the potential use of Rpf-like proteins in detection of a bacterial cell (or diagnosis), treatment, and prophylaxis. For instance, Mukamolova *et al*. (*PNAS* 95: 8916-8921, July 1998 – Applicants' IDS) (Mukamolova *et al*., 1998) stated that it was 'tempting to speculate' that resuscitation and growth of the very significant re-emerging pathogen *Mycobacterium tuberculosis* and possibly of *Mycobacterium leprae* 'may be' controlled in part at least by

members of a family of secreted Rpf-like proteins that function as autocrine and/or paracrine growth factors. See last paragraph in left column on page 8921 of Mukamolova *et al*. (1998). In July 1998, Mukamolova *et al*. concluded as follows [Emphasis added]:

> **Further experimental work will be required to explore these hypotheses**, which may lead, in the short term, to substantially improved laboratory methods **for the detection** and cultivation of these organisms and in the longer term, to therapeutic strategies and vaccines for preventing their growth *in vivo*.

Clearly, Applicants did not describe the invention of the instant claims adequately to show that they had possession of the claimed method that uses the recited genus of polypeptide variants. See e.g., *Noelle v. Lederman*, 355 F.3d 1343, 1348, 69 USPQ2d 1508, 1513 (Fed. Cir. 2004) ('invention is, for purposes of the written description inquiry, *whatever is now claimed*'). Applicants should note that written description requires more than a mere statement that something is a part of the invention and a reference to a potential method for isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd*., 18 USPQ2d 1016. Without a structure-function correlation, the claims do little more than define the claimed invention by function. That is not sufficient to satisfy the written description requirement. *Ex parte Kubin*, 83 USPQ2d 1410 (Bd. Pat. Appl. & Int. 2007) citing *Eli Lilly*, 119 F.3d at 1568, 43 USPQ at 1406 ('definition by function ….. does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is'). The instant claims are viewed as not meeting the written description provision of 35 U.S.C. § 112, first paragraph.

Rejection(s) under 35 U.S.C § 112, Second Paragraph

28) The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his/her invention.

29) Claims 128, 144, 158 and 159 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claim 128, as amended, is indefinite and confusing in the limitations: 'the method identifies a dormant, moribund or latent *Mycobacterium tuberculosis* bacterial cell in the sample'. Claim 128 depends indirectly from claim 126, which includes contacting the bacterial cells with the isolated polypeptide recited therein and incubating the cells in culture medium containing the

polypeptide to resuscitate said cells. It is unclear how a *method of resuscitating* dormant, moribund or latent *Mycobacterium tuberculosis* cells comprising contacting the dormant, moribund or latent *Mycobacterium tuberculosis* cells present in a sample *in vitro* and incubating the cells in culture medium containing the polypeptide ends up being a *method of identifying* specifically 'a dormant, moribund or latent *Mycobacterium tuberculosis* bacterial cell in the sample'.

(b) Claim 128, as amended, is further indefinite and appears to lack proper antecedent basis in the limitation: 'a dormant, moribund or latent *Mycobacterium tuberculosis* bacterial cell in the sample'. Claim 128 depends indirectly from claim 126, which includes the pleural limitation 'dormant, moribund or latent *Mycobacterium tuberculosis* bacterial cells'.

(c) Claim 144 is indefinite because it lacks proper antecedent basis in the limitation: 'cell strain' (see last line). Since line 3 of the claim already includes the limitation, it is suggested that Applicants provide proper antecedent basis by replacing the above-identified limitation with the limitation --the cell strain--.

(d) Claim 159, which depends from claim 128, and claim 158, which depends from claim 144, are also rejected as being indefinite because of the indefiniteness identified above in the base claim.

Remarks

30) Claims 126-128, 131, 144, 148-150 and 157-159 stand rejected.

The amino acid sequences recited at lines 24 and 29 of page 51 of the instant specification are longer than four amino acids in length, yet are not identified by specific SEQ ID numbers as required under 37 C.F.R 1.821 through 1.825.

31) Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. **THIS ACTION IS MADE FINAL.** Applicants are reminded of the extension of time policy as set forth in 37 C.F.R 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

32) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. The Fax number for submission of amendments, responses and/or papers is (571) 273-8300, which receives transmissions 24 hours a day and 7 days a week.

33) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (in USA or CANADA) or 571-272-1000.

34) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, Robert Mondesi, can be reached on (571) 272-0956.

/S. Devi/
Primary Examiner
AU 1645

December, 2009